Office responded to the applicants' enquiry as to the status of the multiple Restriction Requirements pending within the application. Consequently, the applicants respectfully request that the finality of the instant Office Action be withdrawn.

Regarding the subject matter under examination, it seems that there is some confusion. The applicants enquired as to the status of the claims and the ambiguity of the multiple conflicting Restriction Requirements in the last Response. The instant Office Action is not responsive to the applicants' enquiry, and, consequently, the applicants reiterate their enquiry. A Restriction Requirement was made in the Office Action dated June 18, 2002 based on applicants' elected species (Example 19). In the June 18, 2002 Restriction Requirement, the invention was restricted into two groups, Group I, drawn to compounds, compositions, and methods wherein R_1 and R_2 represent H, linear or branched (C_1-C_6)alkyl, aryl, and aryl(C_1-C_6)alkyl in which the alkyl is linear or branched, and Group II, drawn to compounds, compositions, and methods wherein R_1 and R_2 are all other moieties not included in Group I. A second Restriction Requirement was made in the Office Action dated April 9, 2003, which, it is assumed, further restricted the compounds of Group I of the previous Restriction Requirement into Groups I-XII. This second Restriction Requirement involved the substituents "X" and "Y" of Formula I in the generic claim; however, the Restriction Requirement of April 9, 2003 did not provide for the full scope of inventions claimed in the application, i.e., compounds of the original restriction Group I, in part, and compounds of the original restriction Group II. The Office further stated that "applicant's elected species which falls into Group I will be examined. If Group II is prosecuted further in a divisional application, then it may be subject to further restriction." The Office does not make clear to which "Group II" this statement refers. The applicants provide

this overview as a means for clarifying the status of the instant application. Confirmation of the accuracy of this overview and clarification of the noted ambiguity and/or inaccuracy is respectfully solicited. The applicants respectfully request that the Office account for the complete scope of subject matter originally claimed in a final articulation of the Restriction Requirements.

As to the Restriction Requirement of the Office Action dated April 9, 2003, because the restriction does not provide for the full scope of compounds claimed (and exemplified) in the application, we propose, as submitted in the previous Response, the amended definition of "Y" in the Restriction Group I, which is supported by the instant Specification, as follows:

> *"claims 19-34 drawn to a compound of Claim 19 where p and n are as claimed, R_1 and R_2 are H, linear or branched (C_1-C_6)alkyl, aryl, and aryl-(C_1-C_6)alkyl, in which alkyl is linear or branched, X is equal to oxygen or sulphur, Y is equal to pyridyl and C(O)A wherein A represents NR_3R_4 wherein R_3 and R_4 may be identical or different, each represent H or linear or branched (C_1-C_6)alkyl, and pharmaceutical compositions."*

The slightly modified restriction group encompasses the compounds of Examples 2, 4, 11, 14, 18-20, 22-31, 35, and 36; more than six of which compounds were demonstrated to possess significant α_4-$ß_2$ nicotinic binding activity in the LESTAGE Declaration of December 18, 2002. The Claims have been amended to reflect this definition. The Office maintains that the applicants are claiming a compound where radicals such as Y in the compound of Formula I can be as any heteroaryl ring or R_3 and R_4 in A can come together with the nitrogen carrying them to form a monocyclic or bicyclic system. The applicants submit that these radicals in "Y" have been eliminated by the amended definition of "Y" in accord with the above articulated Restriction Group.

The Office maintains its rejection of Claims 19-29 and 31-34 for lack of enablement under 35 USC §112. It is the Office's position that, although "R_1 and R_2 forming together with nitrogen carrying them all 5 to 7 membered saturated carbocyclic systems, Y equal to all heteroaryl(C_1-C_6)alkyl, R_3 and R_4 forming together with the nitrogen carrying them a monocyclic or bicyclical (C_3-C_{10} system) and A equal to all heteroaryl rings" is not in the elected Group I, this phrase is still present in the claims as applicant has not narrowed the claims to the elected subject matter. The applicants submit that the claims were amended on December 18, 2002 to remove the above-mentioned phrase and, therefore, have been narrowed to the elected subject matter and are enabled by the instant specification. Hence, acknowledgement of this amendment, reconsideration, withdrawal of the rejection, and removal of Finality are respectfully solicited.

The Office also maintains rejections of method Claims 31 and 32 under 35 USC § 112, first paragraph. Claim 33 has been amended to claim specific diseases. Applicants submit that the LESTAGE Declaration supports the claim to the treatment of these conditions. Applicants have demonstrated through the LESTAGE Declaration that compounds representative of the claimed invention (Examples 14, 18, 19, 22, 23, 24) have affinity for the central nicotinic receptors associated with these conditions, and that these representative compounds exhibit activity *in vivo* which is characteristic of compounds understood by those skilled in the art to be effective in treating these conditions. Applicants request cancellation of Claims 31 and 32. In view of the fact that applicants have cancelled the method claims directed to the Mechanism of Action and now rely on claims directly drawn to treating specific conditions, reconsideration and withdrawal of the rejection are respectfully requested.

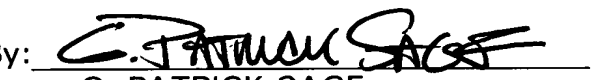
* * * * *

Accordingly, entry of the present amendment, reconsideration of all grounds of objection and rejection, withdrawal thereof, and passage of this application to issue are all hereby respectfully solicited.

It should be apparent that the undersigned attorney has made an earnest effort to place this application into condition for immediate allowance. If he can be of assistance to the Examiner in the elimination of any possibly-outstanding insignificant impediment to an immediate allowance, the Examiner is respectfully invited to call him at his below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,
THE FIRM OF HUESCHEN AND SAGE

By: 
G. PATRICK SAGE

Dated: November 24, 2003
Customer No.: 25,666
500 Columbia Plaza
350 East Michigan Ave.
Kalamazoo, MI 49007-3856
(269) 382-0030

Enclosure: Postal Card Receipt; Listing of Claims.

*****

THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER OR ADDITIONAL FEES WHICH MAY BE REQUIRED (DUE TO OMISSION, DEFICIENCY, OR OTHERWISE), OR TO CREDIT ANY OVERPAYMENT, TO DEPOSIT ACCOUNT NO. 08,3220.

LISTING OF CLAIMS

1-18 (CANCELED)

19 (PRESENTLY AMENDED) A compound selected from those of formula (I) :

(I),

wherein :

p represents an integer of from 0 to 6 inclusive,

n represents an integer of from 0 to 6 inclusive,

R_1 and R_2, which may be identical or different, each independently of the other represent a group selected from hydrogen, linear or branched (C_1-C_6)alkyl, aryl, and aryl-(C_1-C_6)alkyl in which alkyl is linear or branched,

X represents a group selected from oxygen, sulphur, ~~-CH=CH-, methylene, a group of formula -HC=N-O- and a group of formula -O-CH$_2$-CH=CH-, in which groups oxygen is linked to Y of formula (I),~~

Y represents a group selected from pyridyl and ~~aryl, heteroaryl, aryl-(C_1-C_6)alkyl in which the alkyl moiety is linear or branched, heteroaryl-(C_1-C_6)alkyl in which alkyl is linear or branched,~~ -C(O)-A, ~~and -C(S)-A,~~

A represents ~~a group selected from linear or branched (C_1-C_6)alkyl, aryl, heteroaryl, aryl-(C_1-C_6)alkyl in which alkyl is linear or branched, heteroaryl-(C_1-C_6)alkyl in which alkyl is linear or branched, and~~ NR_3R_4 wherein R_3, and R_4, which may be identical or different, each represent a group selected from hydrogen, linear or branched (C_1-C_6)alkyl, ~~aryl, and aryl-(C_1-C_6)alkyl in which alkyl is linear or branched, or R_3+R_4 form together with nitrogen carrying them a monocyclic, or bicyclic (C_3-C_{10}) system,~~

its isomers and addition salts thereof with a pharmaceutically-acceptable acid or base,

~~with the proviso that :~~

~~• *in the case of 1,1-disubstituted compounds of formula (I),*~~

~~-p is other than zero, when X represents methylene, n has the value zero, Y represents~~

~~aryl, or heteroaryl, and R_1, and R_2, which may be identical or different, represent hydrogen, linear or branched (C_1-C_4)alkyl, benzyl, phenylethyl, or form together with the nitrogen carrying them morpholino, thiomorpholino, or a 5- to 7-membered saturated carbocyclic system,~~

~~- p is other than zero, when X represents methylene, n has the value zero, Y represents acetyl, and R_1, and R_2, which may be identical or different, represent hydrogen, linear or branched (C_1-C_4)alkyl, phenyl, benzyl, or form together with the nitrogen carrying them piperidyl, or morpholino,~~

~~- R_1, and R_2 do not simultaneously represent methyl:~~

~~* either, when p, and n each have the value 1, X represents oxygen, and Y is selected from p-nitrobenzoyl, p-aminobenzoyl, p-chlorophenylaminocarbonyl, and acetyl,~~

~~* or, when p has the value zero, n has the value 1, X represents oxygen, or sulphur, and Y represents 2-quinolyl substituted in the 3 position by linear or branched (C_3-C_4)alkyl, or phenyl,~~

~~- Y does not represent 1,2-benzisoxazol-3-yl when n has the value 1, p has the value zero, and X represents oxygen,~~

~~* *in the case of 1,2-disubstituted compounds of formula (I)*,~~

~~- R_1, and R_2 do not simultaneously represent hydrogen when p, and n each have the value zero, and X-Y together represent phenoxy (optionally substituted by one or two, identical or different, groups selected from methoxy, dimethylamino, halogen, methyl, trifluoromethyl, nitro, and amino), phenylsulphanyl, benzyloxy, benzyl, or 2-phenylethyl,~~

~~- R_1 and R_2 do not simultaneously represent methyl when p, and n each have the value zero and X-Y together represent phenoxy (optionally substituted by a group selected from chlorine, and trifluoromethyl), phenylsulphanyl, or benzyl,~~

~~and also with the proviso that the compounds of formula (I) are other than the following compounds :~~

~~- (1-benzylcyclopropyl)methanamine,~~

~~- (1-benzylcyclopropyl)-N,N-dimethylmethanamine,~~

~~- 2-(phenoxycyclopropyl)methanamine,~~

~~- 2-(phenoxymethyl)-cyclopropanamine,~~

~~- (N,N-dimethyl)-2-(acetoxymethyl)-cyclopropanemethanamine,~~

~~- N-{2-[2-(benzyloxy)ethyl]cyclopropyl}-N,N-dimethylamine.~~

it also being understood that :

- aryl denotes phenyl, biphenyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, indanyl, or indenyl, each of those groups being optionally substituted by one or more, identical or different, groups selected from halogen, linear or branched (C_1-C_6)alkyl, hydroxy, cyano, nitro, linear or branched (C_1-C_6)alkoxy, linear or branched (C_2-C_7)acyl, linear or branched (C_1-C_6)alkoxycarbonyl, linear or branched (C_1-C_6)trihaloalkyl, linear or branched (C_1-C_6)trihaloalkoxy, and amino optionally substituted by one or two linear or branched (C_1-C_6)alkyl,

- ~~heteroaryl~~ pyridyl denotes a ~~thienyl~~, pyridyl[[,]] ~~furyl, pyrrolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, pyrazolyl or quinolyl~~ group[[,]] ~~each of those groups being~~ which is optionally substituted by one or more, identical or different, groups selected from substituents defined hereinbefore for aryl.

20 - (PREVIOUSLY PRESENTED) A compound of claim 19, wherein n is an integer of from 0 to 2 inclusive.

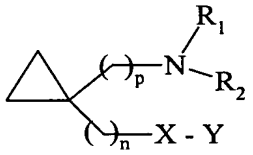
21- (PREVIOUSLY PRESENTED) A compound of claim 19, wherein R_1, and R_2, which may be identical or different, each represent hydrogen, or linear or branched (C_1-C_6)alkyl.

22- (PREVIOUSLY PRESENTED) A compound of claim 19, wherein X represents oxygen.

23- (CURRENTLY AMENDED) A compound of claim 19, wherein Y represents a group selected from -C(O)NR_3R_4 wherein R_3, and R_4, are as defined for formula (I)[[,]] . ~~acetyl, -C(O)-heteroaryl, aryl-(C_1-C_6)alkyl in which alkyl is linear or branched, and heteroaryl.~~

24- (PREVIOUSLY PRESENTED) A compound of claim 19, wherein Y represents pyridyl.

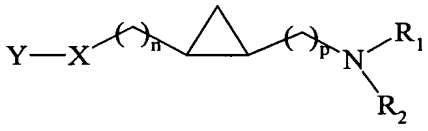
25- (PREVIOUSLY PRESENTED) A compound of claim 19, Which is a compound of formula **(IA)** :



(IA),

wherein n, p, X, Y, R_1 and R_2 are as defined for formula (I), its isomers and addition salts thereof with a pharmaceutically-acceptable acid or base.

26- (PREVIOUSLY PRESENTED) A compound of claim 19, which is a compound of formula **(IB)** :



(IB),

wherein n, p, X, Y, R_1, and R_2 are as defined for formula (I), its isomers and addition salts thereof with a pharmaceutically-acceptable acid or base.

27- (PREVIOUSLY PRESENTED) A compound of claim 19, wherein p is an integer having the value 0 or 1.

28- (CURRENTLY AMENDED) A compound of claim 26, wherein p represents 0, or 1, n represents 0, or 1, R_1 and R_2, which may be identical or different, represent hydrogen, or linear or branched (C_1-C_6)alkyl, X represents oxygen, and Y represents a group selected from ~~phenyl (C_1-C_6)alkyl in which alkyl is linear or branched,~~ pyridyl, and -C(O)-A wherein A represents ~~linear or branched (C_1-C_6)alkyl,~~ mono(C_1-C_6)alkylamino, or di(C_1-C_6)alkylamino, alkyl being linear or branched, its isomers and addition salts thereof with a pharmaceutically-acceptable acid or base.

29- (CURRENTLY AMENDED) A compound of claim 25, wherein p represents 0, or 1, n is an integer of from 0 to 3 inclusive, R_1 and R_2, which may be identical or different, represent hydrogen, linear or branched (C_1-C_6)alkyl ~~or form together with nitrogen carrying them a pyrrolidinyl group~~, X represents oxygen[[,]] or sulphur ~~or CH=CH~~, and Y represents a group selected from ~~phenyl (optionally substituted by hydroxy, linear or branched (C_1-C_6)alkyl or halogen),~~ pyridyl, ~~pyridyl (C_1-C_6)alkyl in which alkyl is linear or branched~~ (pyridyl ~~in each of those groups~~ being optionally substituted by a group selected from halogen, and linear or branched (C_1-C_6)alkyl), and -C(O)-A wherein A represents a group selected from ~~linear or branched (C_1-C_6)alkyl,~~ linear or branched mono(C_1-C_6)alkylamino, and linear or branched di(C_1-C_6)alkylamino, ~~and pyridyl,~~ its isomers and addition salts thereof with a pharmaceutically-acceptable acid or base.

30- (CURRENTLY AMENDED) A compound of claim 19, which is selected from :

- 2-[1-(dimethylamino)cyclopropyl]ethyl methylcarbamate,
- 2-[1-(dimethylamino)cyclopropyl]ethyl dimethylcarbamate,
- [1-(dimethylamino)cyclopropyl]methyl dimethylcarbamate,
- ~~[1-(dimethylamino)cyclopropyl]methyl acetate,~~
- ~~2-[1-(dimethylamino)cyclopropyl]ethyl acetate,~~
- ~~1-[(dimethylamino)methyl]cyclopropyl acetate,~~
- ~~[1-(dimethylamino)cyclopropyl]methyl nicotinate,~~
- *N*,*N*-dimethyl-1-[(3-pyridyloxy)methyl]cyclopropanamine,
- *N*-methyl-1-[(3-pyridyloxy)methyl]cyclopropanamine,
- *N*,*N*-dimethyl-1-[(3-pyridylmethoxy)methyl]cyclopropanamine,
- ~~*N*,*N*-dimethyl-1-[2-(3-pyridyloxy)ethyl]cyclopropanamine,~~
- ~~4-({2-[1-dimethylamino)cyclopropyl]ethyl}sulphanyl)phenol,~~
- (±)-*cis*-2-(dimethylamino)cyclopropyl methylcarbamate,
- (±)-*trans*-2-(dimethylamino)cyclopropyl methylcarbamate,
- ~~(±)-*cis*-2-(dimethylamino)cyclopropyl acetate,~~
- ~~(±)-*trans*-2-(dimethylamino)cyclopropyl acetate,~~
- ~~(±)-*cis*-2-(dimethylamino)cyclopropyl]methyl acetate,~~
- ~~(±)-*trans*-2-(dimethylamino)cyclopropyl]methyl acetate,~~
- ~~(±)-*cis*-2-[(benzyloxy)methyl]-*N*,*N*-dimethylcyclopropanamine,~~

- ~~(±) *trans* 2-[(benzyloxy)methyl] *N*,*N* dimethylcyclopropanamine,~~
- ~~(±) *trans* 2-[(dimethylamino)methyl]cyclopropyl acetate,~~
- 1-[(3-pyridyloxy)methyl]cyclopropanamine dihydrochloride,
- *N*-methyl-1-{[(6-methyl-3-pyridyl)oxy]methyl}cyclopropanamine hydrochloride,
- *N*-methyl-1-{[(6-chloro-3-pyridyl)oxy]methyl}cyclopropanamine hydrochloride,
- *N*-{1-[(3-fluorophenoxy)methyl]cyclopropyl}-*N*-methylamine hydrochloride,
- 3-[1-(dimethylamino)cyclopropyl]propyl dimethylcarbamate fumarate,
- 3-[1-(dimethylamino)cyclopropyl]propyl methylcarbamate fumarate,
- *N*-methyl-1-[(2-pyridylsulphanyl)methyl]cyclopropanamine dihydrochloride,
- *N*-methyl-1-[3-(3-pyridyloxy)propyl]cyclopropanamine dihydrochloride,
- *N*-methyl-1-[2-(3-pyridyl)ethyl]cyclopropanamine dihydrochloride,
- ~~*N* methyl-1-[(Z)-2-(3-pyridyl)ethenyl]cyclopropanamine fumarate,~~
- ~~[1-(1-pyrrolidinyl)cyclopropyl]methyl dimethylcarbamate fumarate,~~
- ~~*N*,*N* dimethyl-1-[2-(3-pyridyl)ethyl]cyclopropanamine hydrochloride,~~
- ~~3-{[1-(1-pyrrolidinyl)cyclopropyl]methoxy}pyridine fumarate,~~
- *N*-methyl-1-[2-(3-pyridyloxy)ethyl]cyclopropanamine fumarate,
- 2-[1-(methylamino)cyclopropyl]ethyl dimethylcarbamate hydrochloride, and
- ~~2-[1-(1-pyrrolidinyl)cyclopropyl]ethyl dimethylcarbamate fumarate,~~

its isomers and addition salts thereof with a pharmaceutically-acceptable acid or base.

31- (CANCELED)

32- (CANCELED)

33- (PRESENTLY AMENDED) A method for treating a living animal body afflicted with age related cognitive disorders and neurodegenerative disorders selected from ~~deficiencies of memory associated with~~ Tourett's Syndrome, Alzheimer's disease, Parkinson's disease, Pick's disease, Korsakoff's disease, ~~or~~ frontal lobe and subcortical dementias, hyperactivity syndrome with attention-deficit, tobacco withdrawal, pain, and mood disorders, comprising the step of administering to the living animal body an amount of a compound of claim 19 which is effective for alleviation of said conditions.

34- (PREVIOUSLY PRESENTED) A pharmaceutical composition comprising as active principle an effective amount of a compound as claimed in claim 19, alone or in combination with one or more pharmaceutically-acceptable excipients or carriers.

35- (CANCELED)

36- (CANCELED)